Company.

AMENDMENT UNDER 37 C.F.R. § 1.121

Please amend the subject Application as follows:

In the Claims:

Cancel claims 19, 23, 33, 44 - 69 and add the following claims 70 through 121.

70. A method of administering a GLP-1 molecule that is protected from the activity of dipetidyl peptidase IV, comprising administering an effective amount of the GLP-1 molecule, or a pharmaceutically acceptable salt thereof, to a patient in need thereof, by pulmonary means.

71. The method of claim 70, wherein the GLP-1 molecule has an amino acid sequence of a formula:

R_1-X-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Y-Gly-Gln-Ala-Ala-Lys-Z-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-R_2

(SEQ ~~ID NO~~:1)

wherein:

R_1 is selected from the group consisting of L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, beta-hydroxy-histidine, homohistidine, alpha-fluoromethyl-histidine, and alpha-methyl-histidine;

X is selected from the group consisting of Gly, Val, Thr, Ile, and alpha-methyl-Ala;

Y is selected from the group consisting of Glu, Gln, Ala, Thr, Ser, and Gly;

Z is selected from the group consisting of Glu, Gln, Ala, Thr, Ser, and Gly; and

R_2 is selected from the group consisting of NH_2, and Gly-OH.

or pharmaceutically-acceptable salts thereof.

72. The method of claim 71, wherein the GLP-1 molecule is selected from the group consisting of Gly^8-GLP-1(7-36)NH_2, Val^8-GLP-1(7-37)OH, alpha-methyl-Ala^8-GLP-1(7-36)NH_2, and Gly^8-Gln^{21}-GLP-1(7-37)OH, or pharmaceutically-acceptable salts thereof.

73. The method of Claim 72, wherein the GLP-1 molecule is Val^8-GLP-1(7-37)OH or a pharmaceutically-acceptable salt thereof.

74. The method of Claim 70, wherein the GLP-1 molecule is delivered to lower airways of the patient.

75. The method of Claim 74, wherein the GLP-1 molecule is deposited in the alveoli.

76. The method of Claim 70, wherein the GLP-1 molecule is inhaled through the mouth of the patient.

77. The method of Claims 70, wherein the GLP-1 molecule is administered as a pharmaceutical formulation comprising the GLP-1 molecule in a pharmaceutically acceptable carrier.

78. The method of Claim 77, wherein the formulation is selected from the group consisting of a solution in an aqueous medium and a suspension in a non-aqueous medium.

79. The method of Claim 78, wherein the formulation is administered as an aerosol.

80. The method of Claim 77, wherein the formulation is in the form of a dry powder.

81. The method of Claim 80, wherein the GLP-1 molecule has a particle size of less than about 10 microns mass median aerodynamic diameter.

82. The method of Claim 81, wherein the GLP-1 molecule has a particle size of about 1 to about 5 microns mass median aerodynamic diameter.

83. The method of Claim 82, wherein the GLP-1 molecule has a particle size of about 2 to about 3 microns mass median aerodynamic diameter.

84. The method of Claims 72, wherein the GLP-1 molecule is administered as a pharmaceutical formulation comprising the GLP-1 molecule in a pharmaceutically acceptable carrier.

85. The method of Claim 84, wherein the formulation is selected from the group consisting of a solution in an aqueous medium and a suspension in a non-aqueous medium.

86. The method of Claim 85, wherein the formulation is administered as an aerosol.

87. The method of Claim 84, wherein the formulation is in the form of a dry powder.

88. The method of Claim 87, wherein the GLP-1 molecule has a particle size of less than about 10 microns mass median aerodynamic diameter.

89. The method of Claim 88, wherein the GLP-1 molecule has a particle size of about 1 to about 5 microns mass median aerodynamic diameter.

90. The method of Claim 89, wherein the GLP-1 molecule has a particle size of about 2 to about 3 microns mass median aerodynamic diameter.

91. The method of Claims 73, wherein the GLP-1 molecule is administered as a pharmaceutical formulation comprising the GLP-1 molecule in a pharmaceutically acceptable carrier.

92. The method of Claim 91, wherein the formulation is selected from the group consisting of a solution in an aqueous medium and a suspension in a non-aqueous medium.

93. The method of Claim 92, wherein the formulation is administered as an aerosol.

94. The method of Claim 91, wherein the formulation is in the form of a dry powder.

95. The method of Claim 94, wherein the GLP-1 molecule has a particle size of less than about 10 microns mass median aerodynamic diameter.

96. The method of Claim 95, wherein the GLP-1 molecule has a particle size of about 1 to about 5 microns mass median aerodynamic diameter.

97. The method of Claim 96, wherein the GLP-1 molecule has a particle size of about 2 to about 3 microns mass median aerodynamic diameter.

98. The method of Claim 70, wherein at least about 10% of the GLP-1 molecule delivered is deposited in the lung.

99. The method of Claim 70, wherein the GLP-1 molecule is delivered from an inhalation device suitable for pulmonary administration and deposited in the lungs of the patient.

100. The method of Claim 99, wherein the device is selected from the group consisting of a nebulizer, a metered-dose inhaler, a dry powder inhaler, and a sprayer.

101. The method of claim 100, wherein the device is a dry powder inhaler.

102. A method for treating a patient with diabetes, comprising administering an effective dose of a GLP-1 molecule, or a pharmaceutically acceptable salt of the GLP-1 molecule, to the patient by pulmonary means, said GLP-1 molecule being protected from the activity of dipetidyl peptidase IV.

103. The method of Claim 102, wherein the GLP-1 molecule has an amino acid sequence of a formula:

R_1-X-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Y-Gly-Gln-Ala-Ala-Lys-Z-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-R_2

(SEQ ID NO:1)

wherein:

R_1 is selected from the group consisting of L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, beta-hydroxy-histidine, homohistidine, alpha-fluoromethyl-histidine, and alpha-methyl-histidine;

X is selected from the group consisting of Gly, Val, Thr, Ile, and alpha-methyl-Ala;

Y is selected from the group consisting of Glu, Gln, Ala, Thr, Ser, and Gly;

Z is selected from the group consisting of Glu, Gln, Ala, Thr, Ser, and Gly; and

R_2 is selected from the group consisting of NH_2, and Gly-OH.

104. The method of Claim 103, wherein the GLP-1 molecule is selected from the group consisting of Gly^8-GLP-1(7-36)NH_2, Val^8-GLP-1(7-37)OH, alpha-methyl-Ala^8-GLP-1(7-36)NH_2, and Gly^8-Gln^{21}-GLP-1(7-37)OH.

105. The method of Claim 104, wherein the GLP-1 molecule is Val^8-GLP-1(7-37)OH.

106. The method of Claim 102, wherein the GLP-1 molecule is delivered from an inhalation device suitable for pulmonary administration and deposited in the lungs of the patient.

107. The method of Claim 106, wherein the device is a sprayer or dry powder inhaler.

108. The method of Claim 106, wherein actuation of the device administers about 40 µg to about 4,000 µg of the GLP-1 molecule.

109. The method of Claim 108, wherein actuation of the device administers about 80 µg to about 2,000 µg of the GLP-1 molecule.

110. The method of Claim 109, wherein actuation of the device administers about 160 µg to about 1,000 µg of the GLP-1 molecule.

111. The method of Claim 110, wherein actuation of the device administers about 320 µg to about 500 µg of the GLP-1 molecule.

112. A method for treating a patient with hyperglycemia, comprising administering an effective dose of a GLP-1 molecule, or a pharmaceutically acceptable salt of the GLP-1 molecule, to the patient by pulmonary means, said GLP-1 molecule being protected from the activity of dipetidyl peptidase IV.

113. The method of Claim 112, wherein the GLP-1 molecule has an amino acid sequence of a formula:

R_1-X-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Y-Gly-Gln-Ala-Ala-Lys-Z-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-R_2

(SEQ ID NO:1)

wherein:

R_1 is selected from the group consisting of L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, beta-hydroxy-histidine, homohistidine, alpha-fluoromethyl-histidine, and alpha-methyl-histidine;

X is selected from the group consisting of Gly, Val, Thr, Ile, and alpha-methyl-Ala;

Y is selected from the group consisting of Glu, Gln, Ala, Thr, Ser, and Gly;

Z is selected from the group consisting of Glu, Gln, Ala, Thr, Ser, and Gly; and

R_2 is selected from the group consisting of NH_2, and Gly-OH.

114. The method of Claim 113, wherein the GLP-1 molecule is selected from the group consisting of Gly^8-GLP-1(7-36)NH_2, Val^8-GLP-1(7-37)OH, alpha-methyl-Ala^8-GLP-1(7-36)NH_2, and Gly^8-Gln^{21}-GLP-1(7-37)OH.

115. The method of Claim 114, wherein the GLP-1 molecule is Val^8-GLP-1(7-37)OH.

116. The method of Claim 112, wherein the GLP-1 molecule is delivered from an inhalation device suitable for pulmonary administration and deposited in the lungs of the patient.

117. The method of Claim 116, wherein the device is a sprayer or dry powder inhaler.

118. The method of Claim 116, wherein actuation of the device administers about 40 µg to about 4,000 µg of the GLP-1 molecule.

119. The method of Claim 117, wherein actuation of the device administers about 80 µg to about 2,000 µg of the GLP-1 molecule.

120. The method of Claim 118, wherein actuation of the device administers about 160 µg to about 1,000 µg of the GLP-1 molecule.

121. The method of claim 119, wherein actuation of the device administers about 320 µg to about 500 µg of the GLP-1 molecule.

Remarks

The Examiner held allowable Claims 19, 23, 33 directed to Val^{8}-GLP-1(7-37)OH species in the Office Action dated June 13, 2000, Paper No. 6. Applicants canceled all other pending claims without prejudice to further prosecute these canceled claims in a continuation application. Additional claims 44 through 69, which originally depended from the genus claims, were amended to depend from the allowed Claims 19, 23, 33 of Val^{8}-GLP-1(7-37)OH species in order to put the Application in condition for allowance. However, in the Office Action dated March 6, 2001, Paper No. 10, the Examiner rejected all claims.

In this response, Applicants have canceled all claims and submit new independent Claims 70, 102, and 112 directed to an intermediate genus of GLP-1 molecules that